REMARKS

Claims 1-19, and 22 are currently pending in the application. Claims 1, 2, 7 and 18 are amended. The amendments find support in the specification and are discussed in the relevant sections below. No new matter is added.

Applicant wishes to thank the Examiner Whisenant for the informal telephone conversation on November 5, 2003 to discuss the outstanding issues.

Rejection of Claims 1-22 under 35 U.S.C. §112, First Paragraph

Claim 22 is rejected under 35 U.S.C. §112, for lack of enablement. The Office Action asserts that the specification "while being enabling for in vitro methods of use, does not reasonably provide enablement for in vivo methods." The Office Action further states that, at the time the application was filed, the prior art taught that gene therapy was unpredictable at best, that one of skill in the art would have to practice undue experimentation to practice the claimed methods, and that, accordingly, the specification does not teach how to practice gene therapy encompassed by the claims. Applicant respectfully disagrees.

Applicant submits that claim 22 claims a method of introducing a biological effector sequence into an organism for the purpose of expressing the biological effector. Thus, the salient issue is whether the claim is enabled for introducing a nucleic acid molecule into an organism, not whether the claim is enabled for introducing and the realizing a biological effect mediated by the introduced biological effector sequence in a gene thereapy setting. Therefore, Applicant submits that, in order to enable claim 22, the components of the claim which need to be enabled are: (1) how to make a biological effector sequence, (2) how to make the nucleic acid molecules of claim 1 or 2, (3) how to introduce the nucleic acid molecules of claim 1 or 2 into a cell and determine whether the nucleic acid molecules have been successfully introduced into a cell, and (4) how to administer this cell into an organism. First of all, Applicant submits that the Examiner has acknowledged that the claims are enabled for *in vitro* methods. Applicant further asserts that

all the components listed above have been described in detail and fully enabled within the specification:

(1) How to make a biological effector sequence: (Please refer to the section entitled Biological effector Sequences Useful According to the Invention, page 14, line 1 – page 17, line 14).

(2) How to make nucleic acid molecules of claim 1 or 2; (For selection of aptamers, please refer to the section entitled Production of Aptamers, page 9, line 24 – page 12, line 2; for production of nucleic acid molecules, please refer to the section entitled Production of Nucleic Acid Molecules, page 12, line 3 – page 13, line 29; for assembly of assembly of bifunctional nucleic acid molecules, please refer to the section entitled Assembly of Bifunctional Nucleic Acid Molecules, page 17, line 15 – page 18, line 25);

(3) How to introduce the nucleic acid molecules of claim 1 or 2 into a cell and determine whether the nucleic acid molecules have been succesfully introduced into a cell; (Please refer to page 25, line 5 – page 27, line 5, page 27, line 14 – page 28, line 2, as well as the sections entitled Compositions that Facilitate Use of Bifunctional Nucleic Acid Molecules, page 22, line 22 – page 24, line 20, and Assay for Gene Transfer, page 18 line 26 – page 22, line 21);

(4) How to administer this cell into an organism; (Please refer to page 27, line 6 – page 27, line 13, and the section entitled Dosage, Mode of Administration, and Pharmaceutical Formulations, page 28, line 3 – page 29, line 29).

The Examiner insists that, because one skilled in the art may take the claimed method and employ the method in an attempt to perform gene therapy, Applicant is required to enable gene therapy. This is not the law. The enablement requirement stipulates that Applicants must teach how to make and use the claimed invention without undue experimentation. As set forth above, Applicant has taught how to make the nucleic acid / aptamer molecules of the invention, how to introduce the molecule into a cell and test for its introduction, and how to introduce the cell into

an organism. This is the extent of Applicant's burden to enable the claimed invention, and Applicant has met this burden.

Applicant submits that ex vivo gene therapy may be one of many downstream uses for claim 22. The fact that one may practice the present invention in the art of gene therapy is not fatal to the enablement of a method for introducing a biological effector sequence into an organism. Applicant notes that, for example, the filing by an inventor of a claim for an expression vector or a method which facilitates the construction of such vectors would have obvious consequences and potential uses in gene therapy, yet would not necessitate enablement in the context of gene therapy. Another example may be claims relating to improved methods of transfection: it is obvious that such methods could be practiced in the art of ex vivo gene therapy, yet the enablement of gene therapy would not be needed. Similar to these hypothetical examples, the present invention is directed to a method of introducing a biological effector sequence into an organism: that such a method may be employed by one skilled in the art in the context of gene therapy does not mean that Applicant bears the burden of enabling gene therapy, and further argues that "the skilled practitioner would have experienced undue experimentation in attempting to practice the claimed invention method of gene therapy". Applicant submits that claim 22 is not a claimed method of gene therapy, but is a method of introducing a biological effector sequence into an organism, a method which would not require undue experimentation to practice.

In conclusion, in light of the fact that all the components of claim 22 are supported and enabled within the specification, Applicant submits that claim 22 is enabled. Applicant therefore respectfully requests withdrawal of the §112, first paragraph rejection and reconsideration of pending claim 22.

Rejection of claims 1-19, 22 under 35 U.S.C. §112, Second Paragraph

Claims 1-19 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Office Action states that the amended claims are confusing in being drawn to a product, a "nucleic aid molecule" and reciting the method step, "wherein the aptamer binds to a cell surface molecule".

Without acquiescing to the rejection, Applicant submits that claims 1 and 2 have been amended. Specifically, the claims claim "an aptamer which binds to a cell surface molecule". Applicant submits that claims 1 and 2, as amended herein, are definite.

The Office Action further states that claims 3-6 lack antecedent basis in claim 1 or 2 for the "third nucleic acid sequence which is an aptamer" because its relationship to the first aptamer is not defined. The Office Action suggests further clarifying the function of the third aptamer.

Applicant submits that claims 3-6 introduce a third component, comprising a second aptamer. Applicant is not clear as to why an antecedent basis is required in this context. It is requested that the Examiner provide further details of the objection if he/she believes there is still a problem with indefiniteness.

The Office Action asserts that claim 7 is confusing because the antecedent of "comprising DNA and RNA" is unclear. It is suggested by the Office Action to clarify which part of the nucleic acid molecule of claim 1 or 2 is DNA and which is RNA.

Applicant has amended claim 7 to: "comprising DNA or RNA". Applicant submits that claim 7, as amended herein, is definite.

Finally, the Office Action states that claim 18 is confusing due to improper Markush group language. It is suggested by the Office Action to recite --claim 1 **and** claim 2-- or, preferably, --a nucleic acid molecule of claim 1, a nucleic acid molecule of claim 2--.

Applicant has amended claim 18 to correct the improper Markush group language. Applicant submits that claim 18, as amended herein, is definite.

With the Amendments summarized above, Applicant submits that all the issues of enablement raised in the previous Office Action have been raised and clarified. Applicant therefore respectfully requests withdrawal of the §112, first paragraph objection and reconsideration of the pending claims.

With this Amendment, Applicant has made an earnest effort to respond to all issues raised in the Office Action of August 26, 2003, and to place all claims presented in condition for allowance. No amendment made was for the purpose of narrowing the scope of any claim, unless Applicant has argued herein that such amendment was made to distinguish over a particular reference or combination of references.

In view of the above, Applicant submits that all issues raised in the Office Action have been addressed herein. Applicant respectfully requests reconsideration of the claims.

Respectfully submitted,

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Name: Kathleen M. Williams
Registration No.: 34,380
Customer No.: 29933
Palmer & Dodge LLP
111 Huntington Avenue
Boston, MA 02199-7613
Tel. (617) 239-0100